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## MICRONUTRIENTS, ACADEMIC PERFORMANCE AND CONCENTRATION OF STUDY: A LITERATURE REVIEW

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**Abstract:** Teenage group include groups who are vulnerable to nutritional problems. at this age group, experienced a rapid growth and development so that the nutritional requirements are also increasing rapidly. Hormonal changes, cognitive, and emotional make adolescent period has become one of the phases that are prone to health problems. The purpose of this paper was to examine the influence of particular micronutrient content of Fe-folate and zinc on the academic performance and the concentration of study in school children. Through literature review, the research found that there is influence between microturient and the academic performance and the concentration of learning in school children. The study recommends examining on a particular age gro  
rient, academic performace, concentration, school children

### INTRODUCTION

Teenage group include groups who are vulnerable to nutritional problems. This age group is experiencing rapid growth and development so that the nutritional requirements are also increasing rapidly. Hormonal changes, cognitive, and emotional make adolescent period has become one of the phases that are prone to health problems (CDPH, 2013). Indirectly, some of the factors that affect adolescents experiencing malnutrition among them are the level of knowledge, the practice of not eating in accordance with the principles of balanced nutrition, social influence, poor sanitation, and technological development (Maziya, 2014). As a result of these factors, many problems arise such as anemia, malnutrition (underweight), growth disorders (short), low productivity that influence achievement, even other disorders caused by deficiency of micronutrients.

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Anemia in school children known to be a public health problem globally reached 25.4% and over 50% had iron deficiency anemia (Iron Deficiency Anemia) (WHO, 2008). In Southeast Asia, according to WHO, the level of IDA in young women from mild to severe reached 15-40%. In other developing countries is also quite high, for example in Yemen reached 34.2%, while in Mexico exceeded 41.6%. In Indonesia, according to the results of Basic Health Research in 2007 (Riskesdas, 2007), the prevalence of anemia among school-age children (5-14 years) reached 9.4% and 70.1% of them suffered from iron deficiency anemia (IDA). In 2013 (Riskesdas, 2013), prevalence of anemia among school children increased in the extreme to 26.4% and more than half experienced IDA. The impact of anemia and IDA are very broad, such as influencing immunity, speed of growth, cognition of children to brain development that affect neurological function and concentration (Ekiz *et al.*, 2005; Guo *et al.*, 2015). DA negative effects on neurological function and intelligence, speed of growth, learning and performance (Igbal *et al.*, 2015).

In addition Fe and folate in relation to anemia and its impact on growth and learning performance, other micro-nutrients of concern and is directly related to the growth and intelligence, namely zinc. Although the data of zinc deficiency in Indonesia seems to be “not yet” available. However, need to watch out the possibility of the prevalence of zinc deficiency. In the northeastern province of Thailand, revealed 70% of school children have low zinc levels, potentially affecting academic ability and their growth (Black 1998; Black 2003; Thurlow *et al.* 2006). Zinc related to somatic growth of children. In addition, zinc is also associated with the endocrine system, which sustains normal growth, secondary sexual characteristics, reproductive function, and thyroid function. Therefore, zinc deficiency causes not only associated with the development, but also sexual maturation, hypogonadism, and thyroid dysfunction (Laitinen 1990; Thurlow *et al.* 2006).

Teens are not only growing in size (the higher or greater), but also functionally progress, especially sexual organs or the “puberty”. During this period, young people need nutrition, not only macro nutrients but also of micronutrients (vitamins and minerals) are more to facilitate hormonal activity in regulating the growth and development of adolescents. According to a new study, teens who consume high amounts of folate in their diet can improve academic achievement (Bourre 2006; Nilsson *et al.* 2011). Other studies have shown that higher folate intake is positively associated with academic achievement in school children aged 15 years, measured by the value of the school at the end of the semester (Nilsson *et al.* 2011). Therefore, the intake of nutrients, especially iron, folic acid, and zinc is very important in the period of children and adolescents.

Iron-fortification of folic acid and zinc can prevent anemia and problems related to physical growth and cognition. Iron-folic acid and zinc fortified can contribute to an increase in hemoglobin (Alarcon *et al.* 2004; Masthalina *et al.* 2012),

development and brain and physical growth (Black 2008; Hermoso *et al.* 2011). Folic acid is able to modify various aspects of DNA such as DNA synthesis, mitosis, and methylation of genes that affect the growth and improvement of human brain function (Igbal, *et al.*, 2015). In addition to folic acid, zinc also has beneficial effects on brain performance. Metabolism and homeostatic conditions, zinc has implications for many processes that involve brain function such as enhancing concentration, as well as to the development of neurodegenerative disorders associated with age. Zinc deficiency also causes Parkinson's disease (a disease that causes decline in brain function in shaping dopamine) (Nriagu, 2007).

Brain development begins during the prenatal period and lasted until school age. Starting with the forming brain cells, followed by migration and differentiation of brain cells and synaptic development that allows cells to communicate with each other so that the function of the brain to work optimally. Folic acid and zinc, including micronutrients that contribute to this mechanism, either directly or indirectly (M. M. Black, 1998; Fernstrom, 2000; Georgieff, 2007). Folic acid is closely related to levels of homocysteine in the blood. If homocysteine is not controlled, it can disrupt the process of development of brain cells. Several studies have concluded that zinc deficiency will affect the long-term growth and intellectual performance through changes in the structure and function of the brain, although the research is limited to animals (M. M. Black, 1998; Chohanadisai *et al.*, 2005).

The intake of micronutrients that support growth, cognitive, and academic achievement can be obtained through the rice fortified with multimikronutrien. Cambodian study on the effects of rice fortification can improve the cognitive abilities of school children as well as reduce the risk of worm infection compared to placebo (Fiorentino *et al.* 2015; Gier *et al.* 2016). Results of other studies conducted on children in India showed that the rice fortification with multiple micronutrients may improve physical ability and concentration of hemoglobin (Thankachan *et al.* 2012; Naido, 2015).

Adequacy of micronutrients including zinc and folic acid can affect the development of cognitive, neuropsychological behavior and motor development. Although this mechanism can not be described in detail but it seems the role of these nutrients in neurogenesis, neuronal migration and synaptogenesis building neurotransmission thereby enhancing the ability of the brain (Bourre 2006; Sen & Kanani 2008; Lehmann *et al.* 2003; Black 1998). Studies in animals show that zinc deficiency during brain development affects cognitive development resulting in decreased ability of the brain, increasing emotional behavior and impair memory (Bhatnagar & Taneja, 2001).

This study examines the relationship between micronutrient particularly containing Fe-folate and zinc to the academic achievement and concentration of study in school children.

## MATERIALS AND METHODS

This study used a literature review approach. The steps taken are to collect information from various sources related to the topic, grouping according to the theme/sub-theme that will strengthen and support the main topic and documented using EndNote program. The next stage is to study literature to ensure that the steps we take are not out of the main topic. The key words are micronutrient, folic acid and zinc, intelligence and learning concentration. A literature search was accredited journals from various sources that provide free articles in pdf format such as PubMed, Proquest, Google Scholar and EBSCO. Other sources were such as books from libraries and national and international health reports, theses and dissertations. We tried to collect literature published in the last 10 years, but if the information is still relevant to the topic, some reference exceeded the time limit of 10 years still we use to enrich the discussion.

## RESULTS

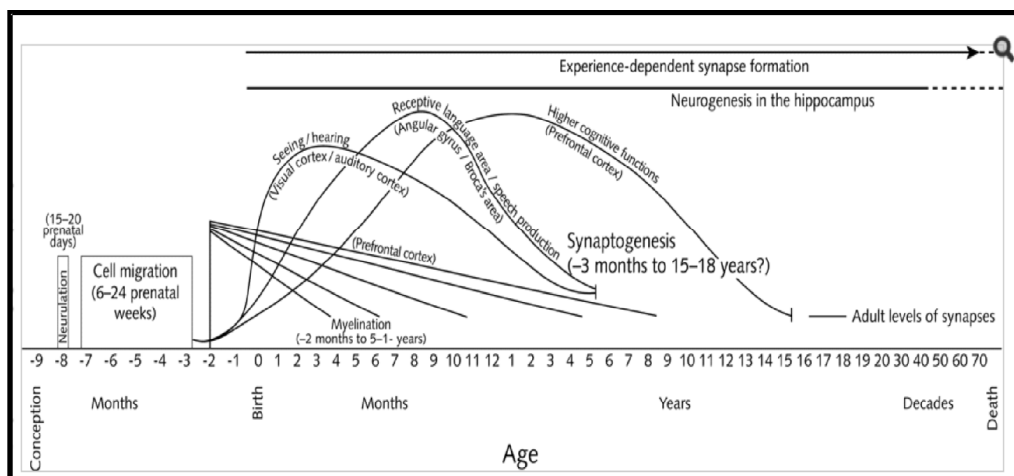
### 1. Folic acid with academic performance and concentration

Adolescence is a vulnerable group to anemic and IDA because of a very rapid growth and puberty which increases the need for iron (Hermoso *et al.*, 2011). It also needs to get serious attention that young women who menstruate will lose a lot of blood, so the rate will need more nutrients, particularly iron (Thane *et al.*, 2003). While folic acid also supports the metabolism of iron and prevent anemia. Therefore, iron-folic acid is needed for the prevention of anemia.

Shortage of certain nutrients such as folic acid is not surprisingly directly affect cognitive development, concentration and energy levels (Wilder, 2012). Seeing role of nutrition is very significant to academic achievement, through the mechanism of anemia, nutritional deficiency of folate and zinc, as well as socioeconomic has a wider coverage. So it is necessary to maintain optimal nutritional status to improve academic performance. According to (Brown *et al.*, 2008), that access to nutrition, especially improving the breakfast habits, can enrich students' psychosocial, discipline, and their cognitive.

Children's intelligence related to many factors such as adequate nutrition, either during pregnancy, after birth, even when the children are studying. Recent research shows that vitamin folic acid can make children smarter, but the mechanism can not be explained in detail. Although the mechanisms underlying the effect of maternal folate status on the development of the neural tube is not well understood, metabolism divided between folate and vitamin B12 shown that a deficiency in the vitamin can change the metabolism of the other. This may be related to the role played by vitamin B12 or in the synthesis of methionine from homocysteine in combination with folic acid (Black 2008).

Brain development begins before birth and continues until school age. It begins with the formation of brain cells, followed by cell migration and differentiation, and development of synapses to allow cells to communicate with one another. Myelin is a network that supports to surround and protect the nerve cells and facilitates communication. Rapid brain growth during the first 2 years of life, especially in the cortex, is associated with higher-order thinking. In addition, the brain myelination, which concentrated on the mid-pregnancy through the second year of life, may be vulnerable to vitamin B12 deficiency. In infants, vitamin B12 deficiency has been linked to demyelination and brain atrophy (Black 2008).



**Figure 1: The development of human brain**

Source: Thompson & Nelson dalam Black (2008)

Critical period of brain growth and development are in the first year. Disorders of the brain in the first year can be permanent damage to the structure and function of the brain. Therefore, therapeutic interventions are required and adequate, either in the form of nutrition and stimulation. Results of studies have shown that children whose mothers took iron supplements and folic acid during pregnancy have a higher intellectual level and motor skills were very good during the years of school age, as well as better organization skills. Iron-Folic acid plays an important role in the growth and development of children, particularly early development of the nervous system. Where the glia cells required for myelination of axons, and grew 10-fold in the first year, especially oligodendrocyte. Glial cell growth depends heavily on iron (Sen & Kanani 2008; Fishman *et al.* 2000).

According to a new study, teens who consume high amounts of folate in their diet can improve academic achievement. Folate and folic acid are forms of vitamin B are water soluble. Folic acid is the synthetic form of this vitamin, while folate occurs naturally in some foods. The researchers found that academic achievement

was significantly associated with high folate intake in the diet and low blood levels of homocysteine. When controlled only folate intake alone, demonstrated a significant relationship with academic achievement (Nilsson *et al.* 2011).

Indirectly, folic acid and vitamins such as B group vitamins and vitamin C are also minerals such as magnesium; manganese and zinc affect brain health. Examples of antioxidants that offer protection from pollution while mineral prevent depression, unfocused and insomnia. Vitamin B6, B12 and folic acid along with niacin (B3) controls a critical process in the body called methylation, which is very important in the formation of almost all neurotransmitters. Neuro transmitter network level (eg, serotonin, dopamine, norepinephrine, and acetylcholine) can be changed, so that changes in neuro anatomy, neurochemistry, or neurometabolic. The functional consequences of these changes vary depending on the particular malnutrition and deficiency of time relative to the neurological development (Holford 2008).

Many of the benefits of folic acid, and is crucial when the brain is still growing and could prevent Alzheimer's in the future (Hooshmand *et al.* 2010). Other studies have shown that higher folate intake is positively associated with academic achievement in adolescent 15 year, measured by the value of the school at the end of the semester. There is a positive correlation between fetal growth, early development and differentiation of the brain in fetuses, breastfeeding and IQ, and better results in a variety of cognitive abilities and academic achievement in children. This effect depends on maternal nutrient intake, and folate as a mediator of positive effects on neurological development. However, the brain continues to develop through childhood and adolescence, and nutritional intake of children themselves will be a major contributor to advance the maturation of the brain, to the potential for scholastic achievement of individuals, although naturally conditioned by background factors as well, such as genetic and socio-economic (Nilsson *et al.* 2011).

## **2. Zinc with academic performance and concentration**

The main effects of zinc deficiency include damage to neuropsychological function. It is for his contributions to the structure and function of the brain (Black 1998). Zinc including substances most widely accumulates in the brain, partly in the hippocampus, amygdala, cerebral cortex and olfactory cortex. Total zinc in the hippocampus estimated 70-90 ppm. Although the majority of zinc in the brain tied as metalloprotein or enzymes, some in the form of zinc or zinc ions or bind weakly and detected by staining reagent (Konoha, *et al.*, 2006).

It is known that zinc is essential to the maturation of the brain and brain function. Zinc deficiency may impair replication outside of cerebellar granule cells and inhibit the relationship between dendrites (Sandstead *et al.* 1998). Zinc

deprivation causes electrophysiological function of the hippocampus becomes abnormal. The nerve cells of the limbic and thoroughly cerebrocortical is rich in zinc. Zinc deficiency causes subtle disturbances in the human neuropsychological performance (Hesse 1979; Sandstead *et al.* 1998).

Zinc contained in the neurotransmitter vesicles in many presynaptic glutamatergic terminals. The release of the neurotransmitter for nerve stimulation would also result in the release of zinc into the synapse (Frederickson & Danscher, 1990). Zinc is also necessary for many homeostatic processes in the brain. Zinc has the potential to act as modulators of excitatory and inhibitory of neurotransmission (Smart *et al.*, 2004). Zinc is also necessary for the production and modulation of melatonin, which helps the dopamine function and is believed to be a key factor in attention and hyperactivity disorders (Chen *et al.*, 1999; Sandyk, 1990). Evidence shows that Zinc likely to be a mediator and modulator key of nerve cell death (Choi & Koh, 1998) because of its role in neurogenesis, neural migration, synaptogenesis, and other neuropsychological disorders (Bhatnagar & Taneja, 2001; Papadopol *et al.*, 2010).

Most zinc body tightly bound to proteins in which he played as a structural or catalytic role. Thus, the release of neurotransmitter for nerve stimulation would also result in the release of zinc into the synapse. Once at the synapse, zinc is able to modulate the activity of postsynaptic glutamate receptors, namely N-methyl-D-aspartate (NMDA) receptors and  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazoles-propionic acid (AMPA). Zinc bind to the NMDA receptor will result in decreased activity while AMPA receptor binding will result in increased activity. This differential activity may be involved in maintaining the integrity of electrical signals through the activation of AMPA receptors while reducing chemical signaling cascade by disabling the NMDA receptor in the presence of middle to high frequency stimulation. This resulted in a lower overall calcium influx, at extreme levels can cause cell death. Thus, the release of zinc usually plays the role of cell-protective. However, excess levels of synaptic zinc can cause cell death. Advantages such as synaptic zinc occurs most often after an ischemic event (Corson, 2015).

Zinc mechanism to cognitive is very complex. Many studies have proven the hypothesis positive role of zinc on the cognitive level of children and adolescents (Black 2003). With good cognitive, student achievement is expected to be better. Based on the above, that is a very high zinc ion concentration in the hippocampus and plays an important role in modulating the spatial learning and memory (Sandstead *et al.* 1998; Yang *et al.* 2013). The expression level of learning and memory associated with synaptic proteins such as receptors and NMDA- NR2A, NR2B, AMPA-GluR1, PSD-93 and PSD-95 was significantly decreased in the hippocampus. Despite the important role of zinc in the hippocampus, especially on memory and BDNF expression, supplementation with high doses of zinc can induce zinc deficiency particular in the hippocampus, which further impair spatial learning

and memory because of the availability of synaptic zinc and deficit reduction in BDNF (Yang *et al.* 2013).

## CONCLUSION AND RECOMMENDATION

There is influence between micronutrient especially Fe-folate and zinc to the academic achievement and concentration at the school children. This study recommends examining further in a specific age.

## References

- Adriani, M., & Wirjatmadi, B. 2012. Peranan gizi dalam siklus kehidupan. *Jakarta: Kencana Perdana Media Group*.
- Ahrens, K., Yazdy, M. M., Mitchell, A. A., & Werler, M. M. 2011. Folic acid intake and spina bifida in the era of dietary folic acid fortification. *Epidemiology*, 22(5), 731-737.
- Alarcon, K. *et al.*, 2004. Effects of separate delivery of zinc or zinc and vitamin A on hemoglobin response, growth, and diarrhea in young Peruvian children receiving iron therapy for anemia. *American Journal of Clinical Nutrition*, 80(5), pp.1276-1282. Available at: <http://search.ebscohost.com/login.aspx?direct=true&AuthType=cookie,ip,cpid&custid=s7324964&db=rzh&AN=2005067660&site=ehost-live&scope=site>.
- Almatsier, S., Soetardjo, S., & Soekatri, M. 2011. Gizi seimbang dalam daur kehidupan. *Jakarta: Gramedia pustaka utama*, 92, 103-105.
- Atikah, P., & Erna, K. 2011. Ilmu gizi untuk keperawatan dan gizi kesehatan. *Yogyakarta: Nuha Medika*, 64-67.
- Audhya, T. 2012. Role of B Vitamins in Biological Methylation. *Health Diagnostics and Research Institute*, 1-20.
- Aunola, K., Stattin, H., & Nurmi, J.-E. 2000. Parenting styles and adolescents' achievement strategies. *Journal of adolescence*, 23(2), 205-222.
- Bhatnagar, S., & Taneja, S. 2001. Zinc and cognitive development. *British Journal of Nutrition*, 85(S2), S139-S145.
- Biesalski, H.-K., Erhardt, J. G., Kraemer, K., & Zimmermann, M. 2007. Diagnosis of nutritional anemia-laboratory assessment of iron status. *Nutritional Anemia*, 37.
- Black, M.M., 2008. Effects of vitamin B12 and folate deficiency on brain development in children. *Food and Nutrition Bulletin*, 29(2 SUPPL.).
- Black, M.M., 2003. Micronutrient Deficiencies and Cognitive Functioning. *J Nutr*, 133, pp.3927-3931.
- Black, M.M., 1998. Zinc deficiency and child development. *Am J Clin Nutr*, 68, pp.464-469.
- Bourre, J.M., 2006. Effects of nutrients (in food) on the structure and function of the nervous system: update on dietary requirements for brain. Part 1: micronutrients. *The journal of nutrition, health & aging*, 10(5), pp.377-385.
- Bridges, K. R., & Pearson, H. A. 2008. *Anemias and other red cell disorders*. New York: McGraw-Hill Medical.



- Brown, K.H., Peerson, J.M. & Allen, L.H., 1998. Effect of zinc supplementation on children's growth: a meta-analysis of intervention trials. *Bibliotheca nutritio et dieta*, (54), pp.76-83.
- Bruner, A. B., Joffe, A., Duggan, A. K., Casella, J. F., & Brandt, J. 1996. Randomised study of cognitive effects of iron supplementation in non-anaemic iron-deficient adolescent girls. *The Lancet*, 348(9033), 992-996.
- CDPH. 2013. *California nutrition and physical activity guidelines for adolescents*.
- Chavasit, V., & Tontisirin, K. 1998. Triple fortification of instant noodles in Thailand. *Food and nutrition bulletin*, 19(2), 164-167.
- Chen, J., Reed, M., Rawlett, A., & Tour, J. 1999. Large on-off ratios and negative differential resistance in a molecular electronic device. *Science*, 286(5444), 1550-1552.
- Choi, D. W., & Koh, J. Y. 1998. Zinc and brain injury. *Annual review of neuroscience*, 21(1), 347-375.
- Chowanadisai, W., Kelleher, S. L., & Lönnerdal, B. 2005. Maternal zinc deficiency reduces NMDA receptor expression in neonatal rat brain, which persists into early adulthood. *Journal of neurochemistry*, 94(2), 510-519.
- Corson, J. 2015. Overview of the Biological Role of Zinc Retrieved September, 2015, from <http://faculty.virginia.edu/metals/cases/corson2.html>
- De Benoist, B., Darnton-Hill, I., Davidsson, L., Fontaine, O., & Hotz, C. 2007. Conclusions of the joint WHO/UNICEF/IAEA/IZiNCG interagency meeting on zinc status indicators. *Food and nutrition bulletin*, 28(3 suppl3), S480-S484.
- de Ungria, M., Rao, R., Wobken, J. D., Luciana, M., Nelson, C. A., & Georgieff, M. K. 2000. Perinatal iron deficiency decreases cytochrome c oxidase (CytOx) activity in selected regions of neonatal rat brain. *Pediatric research*, 48(2), 169-176.
- Drakesmith, H. & Prentice, A., 2008. Viral infection and iron metabolism. , 6(july), pp.541-552.
- Ekiz, C., Agaoglu, L., Karakas, Z., Gurel, N., & Yalcin, I. 2005. The effect of iron deficiency anemia on the function of the immune system. *The Hematology Journal*, 5(7), 579-583.
- Fernstrom, J. D. 2000. Can nutrient supplements modify brain function? *The American Journal of Clinical Nutrition*, 71(6), 1669s-1673s.
- Fiorentino, M. *et al.*, 2015. Rice Fortified with Iron in School Meals Improves Cognitive Performance in Cambodian School Children. , 5(June 2014), pp.769-770.
- Fishman, S.M., Christian, P. & West, K.P., 2000. The role of vitamins in the prevention and control of anaemia. *Public health nutrition*, 3(January), pp.125-150.
- Frederickson, C., & Danscher, G. 1990. Zinc-containing neurons in hippocampus and related CNS structures. *Progress in brain research*, 83, 71-84.
- Georgieff, M. K. 2007. Nutrition and the developing brain: nutrient priorities and measurement. *The American journal of clinical nutrition*, 85(2), 614S-620S.
- Guo, X.-m., Liu, H., & Qian, J. 2015. Daily iron supplementation on cognitive performance in primary-school-aged children with and without anemia: a meta-analysis. *International journal of clinical and experimental medicine*, 8(9), 16107.
- Gier, B. De *et al.*, 2016. Micronutrient-Fortified Rice Can Increase Hookworm Infection Risk/ : A Cluster Randomized Trial., pp. 1-12.

- Hermoso, M. *et al.*, 2011. The effect of iron on cognitive development and function in infants, children and adolescents: A systematic review. *Annals of Nutrition and Metabolism*, 59(2-4), pp.154-165.
- Hesse, G.W., 1979. Chronic zinc deficiency alters neuronal function of hippocampal mossy fibers. *Science (New York, N.Y.)*, 205(4410), pp.1005-1007.
- Holford, P., 2008. *New Optimum Nutrition: Bible*,
- Hooshmand, B. *et al.*, 2010. Homocysteine and holotranscobalamin and the risk of Alzheimer disease: a longitudinal study. *Neurology*, 75(16), pp.1408-1414.
- Hussain, A. 1998. Preventing and controlling micronutrient malnutrition through food-based actions in South Asian countries. *Food, Nutrition and Agriculture (FAO) Alimentation, Nutrition et Agriculture (FAO) Alimentacion, Nutricion y Agricultura (FAO)*.
- Idjradinata, P., & Pollitt, E. 1993. Reversal of developmental delays in iron-deficient anaemic infants treated with iron. *The Lancet*, 341(8836), 1-4.
- Igbal, K., Zafar, T., Igbal, Z., Usman, M., Bibi, H., Afreen, M. S., *et al.* 2015. Effect of Iron Deficiency Anemia on Intellectual Performance of Primary School Children in Islamabad, Pakistan. *Tropical Journal of Pharmaceutical Research*, 14(2), 287-291.
- IZiNCG, I. Z. N. C. G. 2007. *Zinc fortification*.
- Hotz, C. *et al.*, 2008. Efficacy of iron-fortified Ultra Rice in improving the iron status of women in Mexico. *Food and nutrition bulletin*, 29(2), pp.140-149.
- Kanani, S.J. & Poojara, R.H., 2000. Supplementation with Iron and Folic Acid Enhances Growth in Adolescent Indian Girls. *The Journal of Nutrition*, 130, pp.452-455.
- Katelhut, A. *et al.*, 1996. The effects of weekly iron supplementation with folic acid, vitamin A, vitamin C on iron status of Indonesian adolescents. *Asia Pacific J Clin Nutr*, 5(3), pp.181-185.
- Konoha, K., Sadakane, Y., & Kawahara, M. 2006. Zinc neurotoxicity and its role in neurodegenerative diseases. *Journal of health science*, 52(1), 1-8.
- Koutros, S., Zhang, Y., Zhu, Y., Mayne, S. T., Zahm, S. H., Holford, T. R., *et al.* 2008. Nutrients contributing to one-carbon metabolism and risk of non-Hodgkin lymphoma subtypes. *American journal of epidemiology*, 167(3), 287-294.
- Laitinen, R., 1990. Zinc, copper, and sexual maturation in 9-18-year-old girls and boys. *Biological trace element research*, 25(1), pp.71-78.
- Laillou, A., Panagides, D., Garrett, G. S., & Moench-Pfanner, R. 2013. Vitamin A—Fortified Vegetable Oil Exported from Malaysia and Indonesia Can Significantly Contribute to Vitamin A Intake Worldwide. *Food and nutrition bulletin*, 34(2 suppl1), S72-S80.
- Lawless, J.W., KINOTI, S.N. & PERTET, A.M., 1994. Iron Supplementation Improves Appetite and Growth.
- Lehmann, M. *et al.*, 2003. Vitamin B<sub>12</sub>-B<sub>6</sub>-Folate Treatment Improves Blood-Brain Barrier Function in Patients with Hyperhomocysteinaemia and Mild Cognitive Impairment. *Dementia and Geriatric Cognitive Disorders*, 16(3), pp.145-150. Available at: <http://www.karger.com/DOI/10.1159/000071002>.
- Litbangkes. 2007. Riset Kesehatan Dasar 2007. from Badan Penelitian dan Pengembangan Kesehatan Litbangkes. 2013. Hasil Riskesdas 2013.

- Maziya, N. 2014. *Adolescent nutritional status and its association with village-level factors in Tanzania*. Master. Retrieved from scholarworks.umass.edu
- Masthalina, H., Hakimi, M. & Helmyati, S., 2012. Suplementasi multi mikronutrien dibandingkan Fe-asam folat terhadap kadar hemoglobin dan berat badan ibu hamil anemia. *Jurnal Gizi Klinik Indonesia*, (0370), pp.34–40.
- Moretti, D., Zimmermann, M. B., Muthayya, S., Thankachan, P., Lee, T.-C., Kurpad, A. V., *et al.* 2006. Extruded rice fortified with micronized ground ferric pyrophosphate reduces iron deficiency in Indian schoolchildren: a double-blind randomized controlled trial. *The American Journal of Clinical Nutrition*, 84(4), 822-829.
- Murakami, K. *et al.*, 2010. Dietary intake of folate, vitamin B6, vitamin B12 and riboflavin and risk of Parkinson's disease: a case-control study in Japan. *The British journal of nutrition*, 104(5), pp.757–764.
- Nesamvuni, A. E., Vorster, H. H., Margetts, B. M., & Kruger, A. 2005. Fortification of maize meal improved the nutritional status of 1–3-year-old African children. *Public health nutrition*, 8(05), 461-467
- Nilsson, T.K. *et al.*, 2011. High folate intake is related to better academic achievement in Swedish adolescents. *Pediatrics*, 128(2), pp.e358–e365.
- Nriagu, J. 2007. Zinc deficiency in human health. *School of Public Health*.
- Papadopol, V., Tuchendria, E., & Palamaru, I. 2010. Zinc levels, cognitive and personality features in children with different socioeconomic backgrounds. *Europe's Journal of Psychology*, 6(1), 82-101.
- Puspaningtyas, D. E., Sudargo, T., & Syamsiatun, N. H. 2012. Hubungan Status Anemia, Praktik Pemberian Makan, Praktik Perawatan Kesehatan, Dan Stimulasi Kognitif Dengan Fungsi Kognitif Anak Sekolah Dasar. *Gizi Indonesia*, 2(35).
- Radhika, M. S., Nair, K. M., Kumar, R. H., Rao, M. V., Ravinder, P., Reddy, C. G., *et al.* 2011. Micronized ferric pyrophosphate supplied through extruded rice kernels improves body iron stores in children: a double-blind, randomized, placebo-controlled midday meal feeding trial in Indian schoolchildren. *The American Journal of Clinical Nutrition*, 94(5), 1202-1210.
- Ranasinghe, A., Johnson, N., Scragg, M., & Williams, R. 1989. Iron deficiency reduces cytochrome concentrations of mitochondria isolated from hamster cheek pouch epithelium. *Journal of Oral Pathology & Medicine*, 18(10), 582-585.
- Ratledge, C., 2007. Iron metabolism and infection. *Food and nutrition bulletin*, 28(4 Suppl), pp.S515–23.
- Romano, P. S., Waitzman, N. J., Scheffler, R. M., & Pi, R. D. 1995. Folic acid fortification of grain: an economic analysis. *American journal of public health*, 85(5), 667-676.
- Sandyk, R. 1990. Zinc deficiency in attention-deficit hyperactivity disorder. *International Journal of Neuroscience*, 52(3-4), 239-241.
- Sandstead, H.H. *et al.*, 1998. Effects of repletion with zinc and other micronutrients on neuropsychologic performance and growth of Chinese children. *American Journal of Clinical Nutrition*, 68(2 SUPPL), 470–475.
- Sen, A. & Kanani, S., 2012. Intermittent iron folate supplementation: impact on hematinic status and growth of school girls. *ISRN hematology*, 2012, p.482153. Available at: /pmc/articles/PMC3412096/?report=abstract.

- Sen, A. & Kanani, S.J., 2008. Impact of iron-folic acid supplementation on cognitive abilities of school girls in Vadodara. *Indian pediatrics*, 46(2), pp.137-143.
- Silva, A.P.R. et al., 2006. Effects of zinc supplementation on 1- to 5-year old children. *Jornal de pediatria*, 82(3), pp.227-31. Available at: [http://www.jped.com.br/conteudo/Ing\\_resumo.asp?varArtigo=1480&cod=&idSecao=4](http://www.jped.com.br/conteudo/Ing_resumo.asp?varArtigo=1480&cod=&idSecao=4) \n<http://www.ncbi.nlm.nih.gov/pubmed/16738738>.
- Singh, R., Kanwar, S. S., Sood, P. K., & Nehru, B. 2011. Beneficial effects of folic acid on enhancement of memory and antioxidant status in aged rat brain. *Cellular and molecular neurobiology*, 31(1), 83-91.
- Smart, T. G., Hosie, A. M., & Miller, P. S. 2004. Zn<sup>2+</sup> ions: modulators of excitatory and inhibitory synaptic activity. *The Neuroscientist*, 10(5), 432-442.
- Soliman, A.T., De Sanctis, V. & Kalra, S., 2014. Anemia and growth. *Indian Journal of Endocrinology and Metabolism*, 18(Suppl 1), pp.S1-5.
- Thane, C., Bates, C., & Prentice, A. 2003. Risk factors for low iron intake and poor iron status in a national sample of British young people aged 4-18 years. *Public health nutrition*, 6(05), 485-496.
- Thankachan, P. et al., 2012. Multiple Micronutrient-Fortified Rice Affects Physical Performance and Plasma Vitamin B-12 and Homocysteine Concentrations of Indian. *The Journal of nutrition*, 142, pp.846-852.
- Theary, C., Panagides, D., Laillou, A., Vonthanak, S., Kanarath, C., Chhorvann, C., et al. 2013. Fish sauce, soy sauce, and vegetable oil fortification in Cambodia: Where do we stand to date? *Food and nutrition bulletin*, 34(2 suppl1), S62-S71.
- Naido, P. 2015. Evaluation of clinics on the provision of youth friendly services in the Ethekwini Metro of Kwazulu Natal. *International Journal of Health and Medical Sciences*, 1(1), 1-7.
- Thompson, B. & Amoroso, L., 2010. Combating Micronutrient Deficiencies/ : Food-based Approaches. *Agriculture*, pp.1-14.
- Thurlow, R.A. et al., 2006. Risk of zinc, iodine and other micronutrient deficiencies among school children in North East Thailand. pp. 623-632.
- UNICEF. 1998. *Conceptual framework for nutritional status*.
- Veena, S. R., Krishnaveni, G. V., Srinivasan, K., Wills, A. K., Muthayya, S., Kurpad, A. V., et al. 2010. Higher maternal plasma folate but not vitamin B-12 concentrations during pregnancy are associated with better cognitive function scores in 9-to 10-year-old children in South India. *The Journal of nutrition*, 140(5), 1014-1022.
- Weinberg, E.D., 1977. Infection and iron metabolism. *The American Journal of Clinical Nutrition*, 30(9), pp.1485-1490. Available at: <http://ajcn.nutrition.org/content/30/9/1485.abstract>.
- WHO, 2011. *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity*, Available at: <http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Haemoglobin+concentrations+for+the+diagnosis+of+anaemia+and+assessment+of+severity#1>.
- WHO. 2008. Iron deficiency anemia Retrieved Agustus, 2015, from [www.who.int](http://www.who.int)
- WHO, 2001. *Iron deficiency anemia assessment, prevention, and control*.
- Widjojo, S.R., 2014. Fortifikasi Beras/ : Review Pengalaman di Berbagai . , pp.1-41.

Wilder, R. 2012. Homeless Children and Their Families Retrieved 15 September, 2015, from [www.wilder.org](http://www.wilder.org)

Yang, Y. *et al.*, 2013. High Dose Zinc Supplementation Induces Hippocampal Zinc Deficiency and Memory Impairment with Inhibition of BDNF Signaling. *PLoS ONE*, 8(1).